

## **REMARKS**

Restriction is required in the above-identified application due to alleged lack of unity of invention. According to the examiner, the currently pending claims, which are directed to screening methods for Tau protein phosphorylation inhibitors, substances obtained by such method and a method of treating taupathy, encompass seven (7) separate, patentably distinct inventions, as set forth at page 3 of the Official Action.

The March 13 Official Action also includes separate election of species requirements with respect to Tau phosphorylation sites (40 distinct species) and phosphorylation detection (two distinct species).

For the reasons presented below, applicants respectfully traverse and request reconsideration of the requirements for restriction and election of species set forth in the March 13, 2008 Official Action.

It is noted preliminary that a claim amendment is presented with this response in which claim 22 is amended to incorporate the subject matter of original claim 30. Claim 36 is amended to state that the step recited therein is a further step, relative to the method of claim 22, in which a determination is made of whether, and optionally to what extent, the candidate substance inhibits the phosphorylation of another substrate by the casein kinase 1, thus incorporating the subject matter of original claim 37.

Claims 30, 37 and 50-52 have been cancelled in accordance with this amendment.

The cancellation of these claims is without prejudice to applicants' right to file one or more continuation applications with respect to the subject matter thereof, as provided in 35 USC §120.

No new matter has been introduced into this application by reason of the present claim amendment, entry of which is respectfully requested.

Applicants take exception to the examiner's contention that the claims lack unity of invention in violation of PCT Rule 13.1. It is respectfully submitted that the claims as presently amended are unified under the requirements of the PCT.

### **A. Claim 22 and its Dependent Claims**

Claim 22 as currently amended recites a method of screening for substances which are capable of inhibiting phosphorylation of a tau protein by CK1, involving the step of determining whether, and optionally the extent to which, the candidate substance inhibits the phosphorylation of tau at one or more sites of the tau protein by CK1, wherein the CK1

phosphorylates the tau protein at one or more of a group of specific phosphorylation sites recited in the claim. The method of the present invention is particularly useful as it is based on the identification by the present inventors of sites which are phosphorylated by CK1 in the absence of other kinases (see Table 2). These sites are now listed in the claim. The identification that these sites are phosphorylated by Tau in the absence of other kinases allows the identification of CK1 specific inhibitors by the screening method of the present invention.

The examiner will appreciate that the identification of CK1 specific inhibitors provides numerous advantages, including the identification of substances which may be useful in the treatment of Alzheimer's Disease (AD) and other related tauopathies (see page 8 lines 29-31 of the instant application), and providing a platform for further studies into the mechanism of AD and other related diseases, for example as discussed at page 40 of the instant application.

The examiner alleged that the shared technical feature of Groups I to VII is a method of screening for substances that inhibit tau phosphorylation by CK1, and that this technical feature is shown, by Kuret et al., to lack novelty or inventive step. In the claims as currently amended, the shared technical feature is at least a method for screening substances which inhibit Tau phosphorylation by CK1 at specified phosphorylation sites.

The disclosure of Kuret et al. is concerned with providing data which may imply that CK1 $\alpha$  isoforms are involved in the formation of hyperphosphorylated tau in neurodegenerative disease, for example due to the tight association of these isoforms with tau pathology. The conclusions reached in this reference are presented as speculative or putative conclusions: the presented data are said to be "consistent with" CK1 $\alpha$  playing a role in tau phosphorylation. For example, at page 2513, left column lines 41-43 it is stated that "the subcellular distribution of CK1 $\alpha$  immunoreactivity is consistent with a role in tau phosphorylation".

In addition to the speculative tone of Kuret et al., it is noted that nowhere in this reference is the screening method for inhibitors of tau phosphorylation by CK1 disclosed or even contemplated. Additionally, there is no disclosure or suggestion of a method for detecting phosphorylation of tau by CK1 at specific sites in the Tau protein, nor of sites which allow for the detection of phosphorylation by CK1 in the absence of other kinases. Furthermore, there is certainly no disclosure of the particular specific sites recited in claim 22, nor a method of screening for an inhibitor of phosphorylation of tau by CK1 at

these sites. Likewise, none of these features is disclosed by Singh et al. Therefore, the shared technical feature of the claims is not disclosed or suggested in the cited references.

For the above-stated reasons, it can be seen that the shared technical feature of the claims is novel and non-obvious when considered in light of the prior art. Therefore, the subject matter of claim 22 and its dependent claims are linked by a single inventive concept as required by PCT Rule 13.1. The restriction requirement dividing claim 22 among Groups I-III should, therefore, be withdrawn.

#### **B. Other Claims**

Regarding the other claims, it is noted that claims 50 to 52 have been deleted in the claim set currently presented. Claim 46, directed to a substance obtained by the method of claim 22 is unified with the currently presented claims as it is produced by a method employing the special technical feature. In addition, it provides the same advantages as the method, for example in the treatment of AD and related diseases, and in the investigation of the mechanism of such diseases. Claims 53 and 54 are directed to methods of medical treatment employing a substance obtained by the method of claim 22. These claims also are unified with the other claims currently presented, as they have the same technical feature and advantages as discussed above. Claim 45 is unified with the other claims for similar reasons.

In order to be fully responsive to the above-mentioned restriction and election of species requirements, applicants provisionally elect, with traverse, for examination in this application the subject matter of Group II, i.e., claims 22-32, 36-42 and 51 drawn to a method of screening for inhibitors of Tau protein phosphorylation by a kinase including CK1 using a substrate other than Tau protein, and further elect the species S289 (designated site (q) in the March 13 Official Action), and mass spectroscopy for phosphorylation detection. Claims 22-29, 32, 36 and 38-42 are believed to read on the elected subject matter.

Applicants' elections in response to the present restriction and election of species requirements are without prejudice to their right to file one or more divisional applications, as provided in 35 USC §121, on the subject matter of any claims finally held withdrawn from consideration in this application.

Turning to another aspect of the March 13 Official Action, the requirement that applicants submit an amendment directing entry of the substitute sequence listing paper copy into the specification appears unwarranted. It is noted in this regard that the fourth sentence of the second paragraph of the Reply to Official Communication and Submission of Sequence

Listing Under 37 CFR §§1.821-1.825, filed September 24, 2007, specifically states that “Applicants respectfully request entry of the sequence listing into the above identified patent application”. Thus, it is believed that applicants have already satisfied the requirements of Rules 821-825 relating to the submission of a sequence listing.

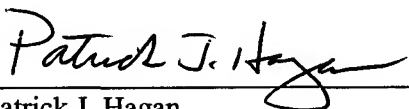
Lastly, it is noted that an initial shortened statutory period of one (1) month was set in the March 13, 2008 Official Action. The initial due date for response, therefore, was April 13, 2008. A petition for a three (3) month extension of the response period is included with this Second Preliminary Amendment and Traversal of Requirements for Restriction and Election of Species, which is being filed before the expiration of the three (3) month extension period.

Early and favorable action on the merits of this application is respectfully requested.

Respectfully submitted,

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